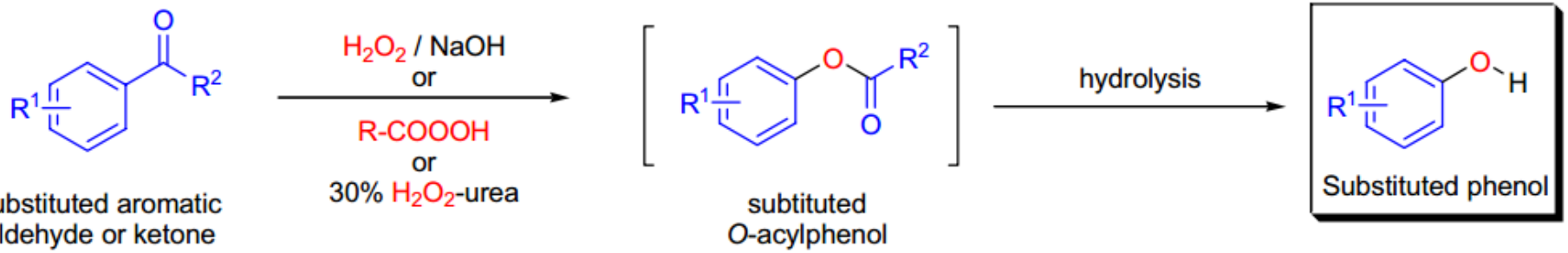
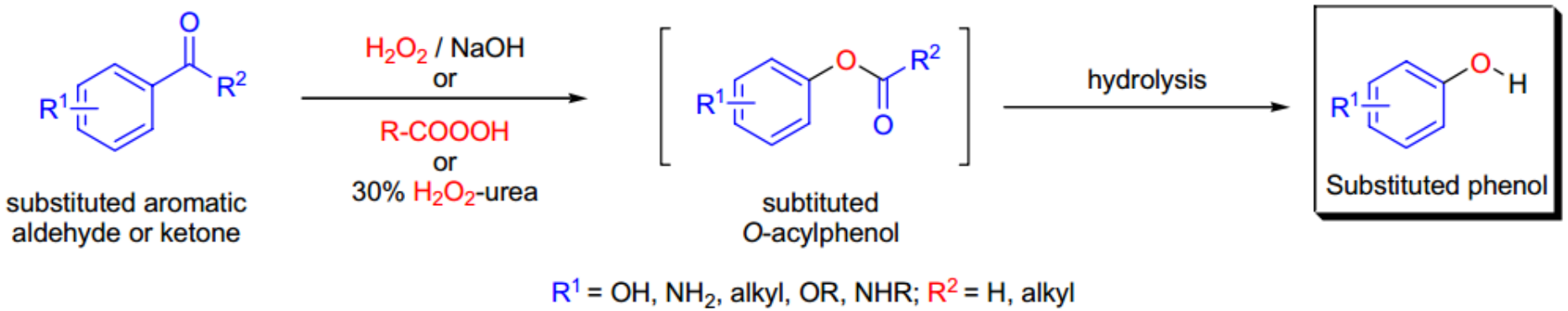
DAKIN OXIDATION



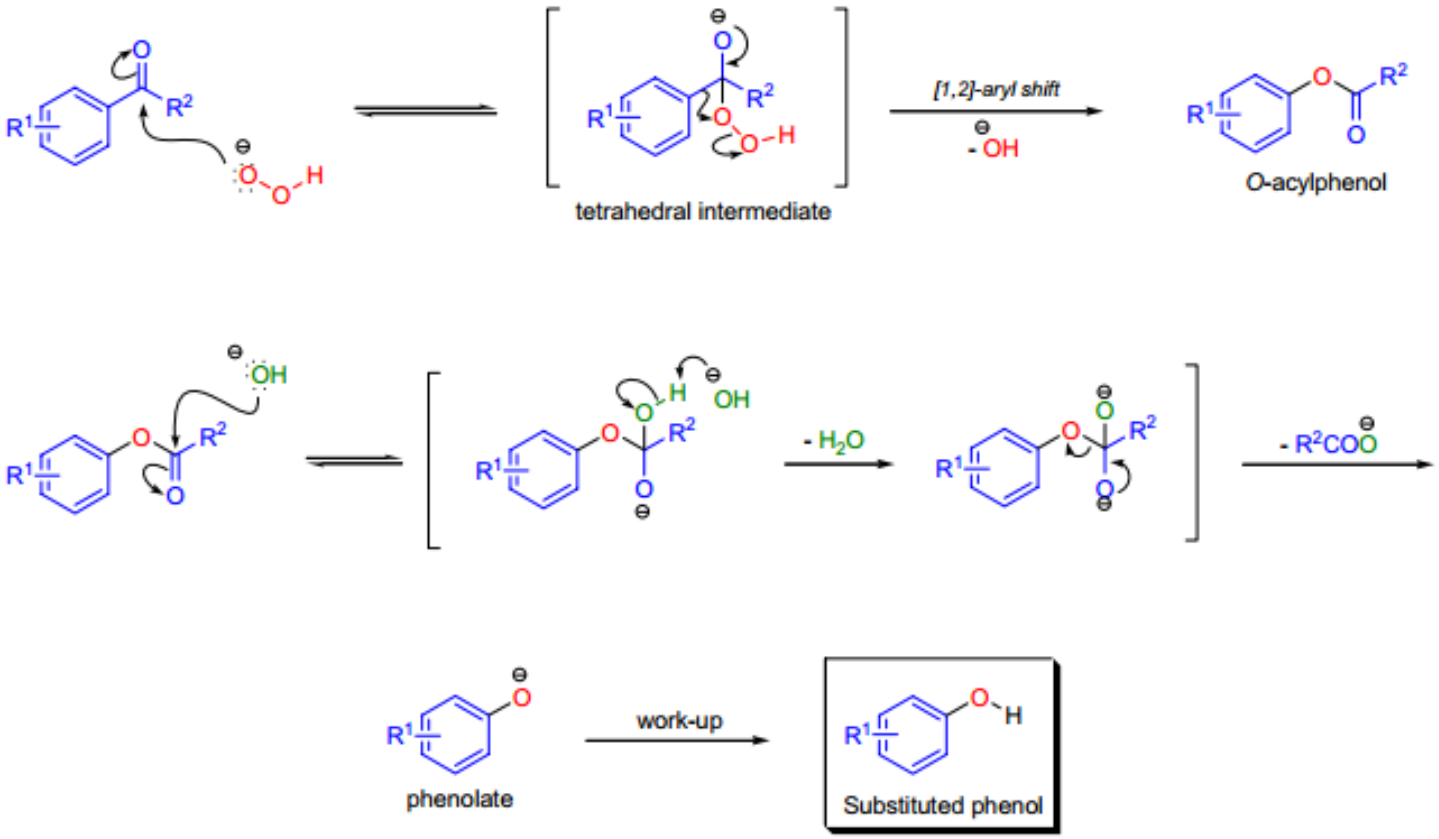
R^1 = OH, NH_2, alkyl, OR, NHR; R^2 = H, alkyl



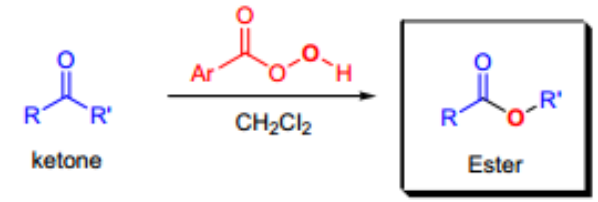
R^1 = OH, NH_2, alkyl, OR, NHR; R^2 = H, alkyl

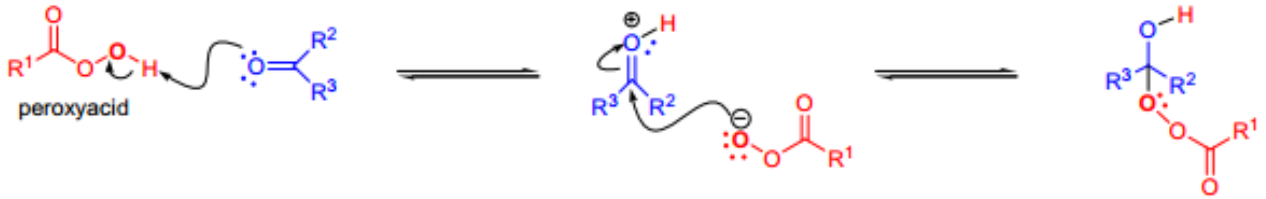
- The reaction works best if the aromatic aldehyde or ketone is electron rich (-R, -OH, -OR, -NH2, or -NHR substituents in the ortho or para positions).
- When the aromatic ring is substituted with electron-withdrawing groups, the product of the oxidation is usually the carboxylic acid.
- Consequently, oxidation accelerates as pH increases toward the pKa of hydrogen peroxide and hydroperoxide concentration climbs. At pH higher than 13.5, oxidation does not occur.

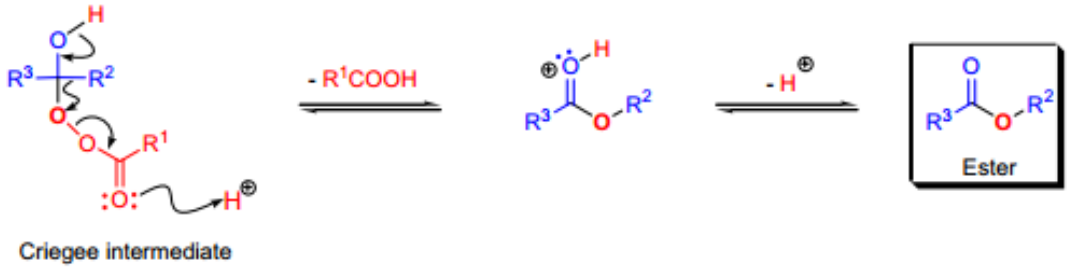
Mechanism:

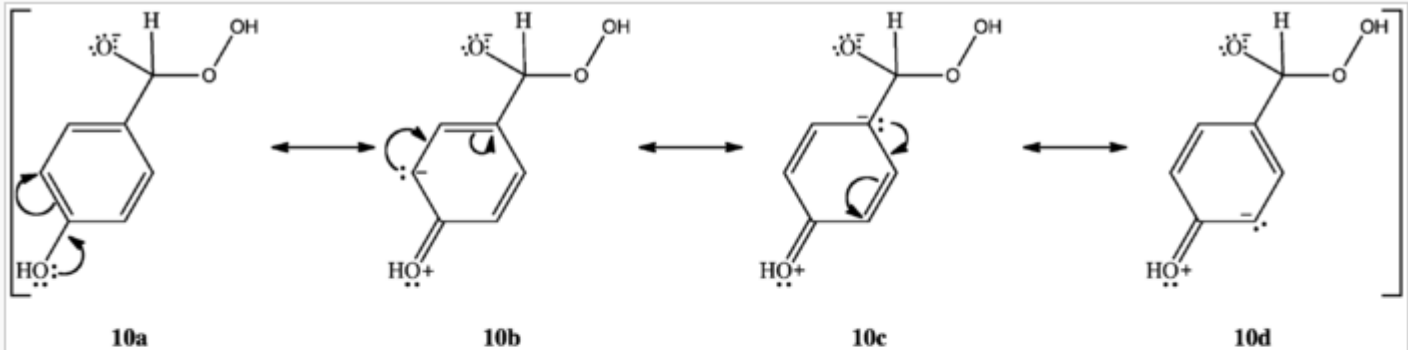

[1,2]-aryl shift
- OH
tetrahedral intermediate
O-acylphenol
- H2O
- R2COO
work-up
phenolate
Substituted phenol

BAEYER-VILLIGER OXIDATION/REARRANGEMENT

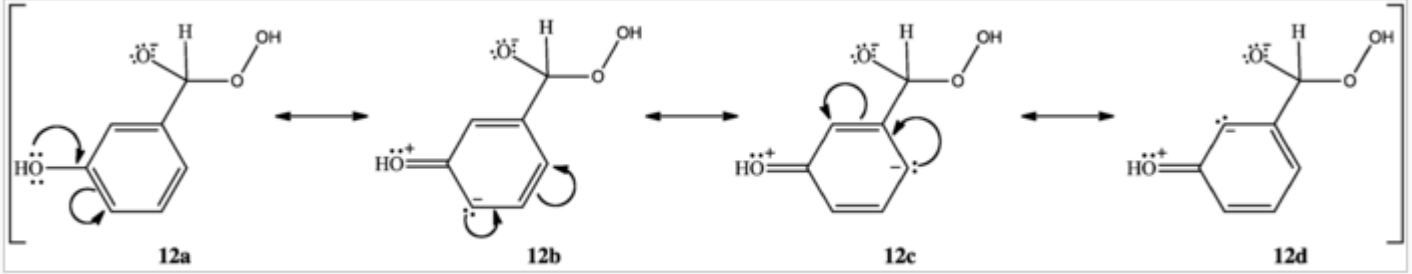






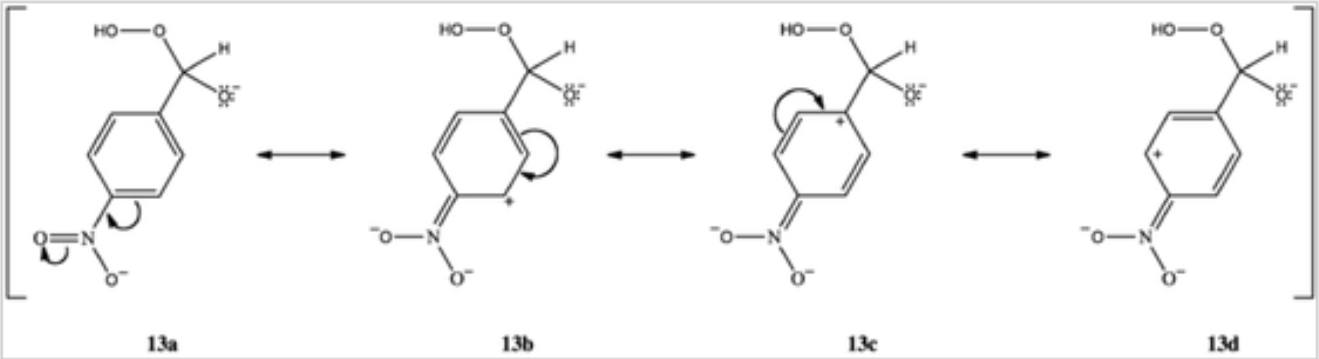


Concentration of electron density at the migrating carbon with *para* (top) and *ortho* (bottom) hydroxyl group



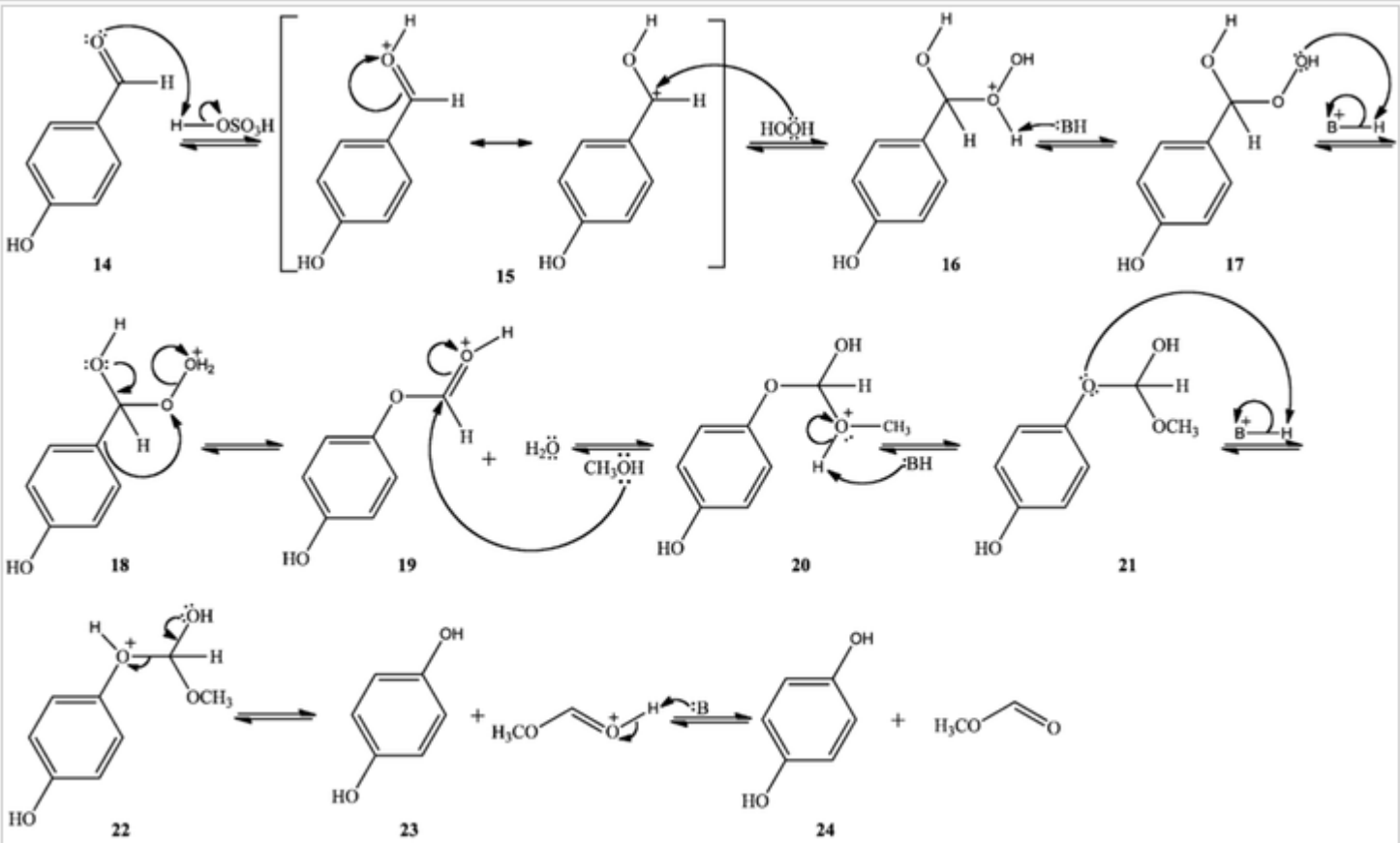
Lack of electron density concentration at the migrating carbon with *meta* hydroxyl group

Concentration of positive charge at migrating carbon with para nitro group



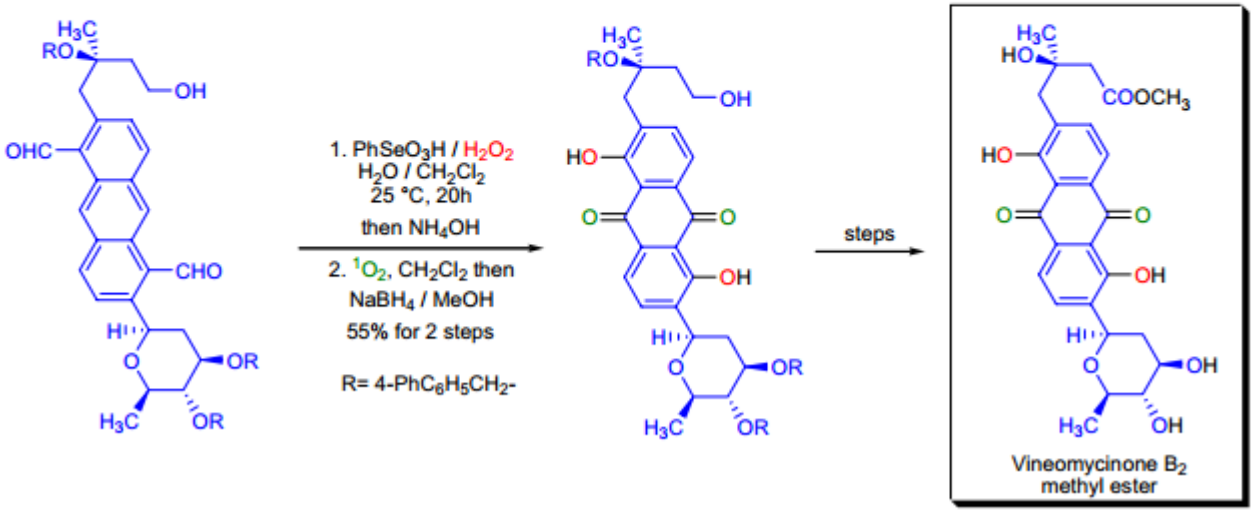
Concentration of positive charge at migrating carbon with *para* nitro group

Acid-catalyzed Dakin oxidation mechanism



Acid-catalyzed Dakin oxidation mechanism

The total synthesis of vineomycinone B_2 methyl ester was accomplished in the laboratory of C. Mioskowski using a *double Bradsher cyclization*, a *modified Dakin oxidation*, and a *singlet oxygen oxidation* as key steps.[18] The substituted anthracene-dialdehyde derivative was treated under *modified Dakin oxidation* conditions, that is, with phenylselenic acid and hydrogen peroxide at 20 °C for 20h, to introduce the phenolic oxygens. This was followed by a singlet oxygen addition across the central aromatic ring with reductive work-up and air oxidation to generate the desired anthraquinone functionality.



Carboxy-functionalized fluorescein dyes are important as conjugated fluorescent markers of biologically active compounds. M.H. Lyttle et al. have used the *Dakin oxidation* on 4-methoxy-3-hydroxy-2-chloro-benzaldehyde to obtain the desired resorcinol derivative that served as an intermediate in their improved synthesis.[20]